OPINION

by Assoc. Prof. Natasha Danova, MD,

on the dissertation

"ACCESS TO GENE AND CELL THERAPIES AS INNOVATIVE HEALTH TECHNOLOGIES IN BULGARIA",

by Dr. Stamen Georgiev Bankovski – part-time doctoral student at the National Center for Public Health and Analyses (NCPHA) for the award of the academic and scientific degree of "Doctor"

The significance of access to gene and cell therapies is multifaceted—clinical, social, economic, and health policy-related. Like many other complex modern health technologies, they present both scientific and regulatory challenges. Improving health outcomes and addressing unmet needs are among the key priorities of any modern healthcare system. This makes potential problems with access to gene and cell therapies a key scientific and practical priority, because they often target severe, rare, or life-threatening diseases for which there are no effective alternatives. Limited access means a direct loss of health benefits for patients. The dissertation emphasizes that lack of access also leads to enormous social injustice—patients with financial means or access to treatment abroad can receive therapy, while others are left without treatment.

The role and importance of the healthcare system and its policies are immense, because access to innovative therapies serves as an indicator of: the healthcare system's effectiveness; its ability to adopt innovations; and its level of alignment with European practices. Limited access creates a risk of falling behind other countries.

The economic and resource implications of gene and cell therapies are also significant, as they are associated with: high costs; single-use applications; and substantial budgetary pressure. Therefore, access to them requires innovative financial and organizational models that balance sustainability with patient needs.

This specific group of medicinal products is of strategic importance for the future of medicine. The situation is critical because the number of these therapies is growing, and they will become an increasingly important part of treatment in fields such as oncohematology and rare diseases, yet the payment for these expensive therapies remains a global problem.

The dissertation includes all necessary components: an introduction, 4 chapters: literature review, aim and objectives, materials and methods, analysis of results, discussion of results, limitations, conclusions, recommendations, and contributions. It is presented on 133 pages, is illustrated, and contains 16 figures and 18 tables. The bibliography includes 201 contemporary literature sources.

The introduction emphasizes the importance of access to gene and cell therapies as a key factor in improving health outcomes, reducing inequalities, and modernizing the healthcare system.

The first chapter is a comprehensive and well-structured literature review focused on a systematic examination of the current scientific and regulatory aspects of gene and cell therapies, with an emphasis on their accessibility, efficacy, and role in healthcare systems. The development and characteristics of gene and cell therapies are traced. The basic principles, mechanisms of action, and clinical applications of ATMPs are examined, including their positioning in modern medicine. Special attention is given to the regulatory framework and authorization procedures. European and international regulations are analyzed, including the processes for marketing authorization, quality assessment, safety, and efficacy. Access to and reimbursement for gene and cell therapies are described in detail, with a particular emphasis on: payment mechanisms; health technology assessment (HTA); and the challenges associated with high costs and limited budgets.

In the literature review, the doctoral student identifies as key barriers: elevated pharmacoeconomic indicators affecting the sustainability of health systems, and specific ethical issues and moral aspects. The challenges to implementation are defined as: logistical constraints; lack of expertise; and regulatory and administrative difficulties. The review concludes with a summary of the available advanced therapy medicinal products (ATMPs) in Bulgaria. Despite significant scientific progress and the availability of approved ATMPs in Europe.

Their actual availability in our country remains limited, which underscores the need to improve regulatory, financial, and organizational mechanisms within the healthcare system.

The second chapter outlines the study methodology, defining the objective, tasks, and methods used, as well as the study design and data sources. The main objective is clearly stated: "to conduct a comprehensive analysis of access to gene and cell therapies as innovative health technologies in Bulgaria, assessing the regulatory, organizational, and financial pathway from obtaining marketing authorization to actual application in patients." A secondary objective has also been set, which is very practically oriented: "to develop an applicable model(s) for sustainable financing, adapted to the Bulgarian context and compatible with European regulatory and HTA frameworks." There are 7 tasks, which logically follow from the objective. The study design is correctly defined, and the data sources have been selected. The literature search was conducted in the world-renowned bibliographic databases PubMed/MEDLINE, Scopus, and Web of Science.

The methodology of the dissertation research is based on a comprehensive, multi-method approach combining quantitative and qualitative methods for analyzing access to ATMPs in Bulgaria.

The study includes a retrospective analysis of available ATMPs at the European and national levels, examining approved therapies, their regulatory status, and their degree of inclusion in the national reimbursement system. Data from official infrastructure and expertise for implementation; information—limited awareness and lack of sufficient data

The pharmacoeconomic analysis shows that traditional cost-effectiveness evaluation approaches are difficult to apply to these therapies due to their high cost, small patient populations, and uncertainty regarding long-term effects. This necessitates the introduction of innovative payment models (e.g., outcomes-based).

In addition, the comparative analysis conducted by the doctoral candidate with other European countries shows that Bulgaria lags behind in terms of timely access to innovative therapies, which places patients at a disadvantage.

In the fourth chapter, "Discussion of the Results," the dissertation interprets the identified barriers to access to ATMPs in the context of existing European practices and the scientific literature. It emphasizes that the problems observed in Bulgaria are not isolated but are more pronounced due to the specificities of the healthcare system, including limited financial resources and administrative capacity.

The discussion focuses on the mismatch between the innovative nature of ATMPs and traditional models of evaluation and financing, which are not fully applicable to therapies that are high-cost, single-use, and uncertain in terms of long-term efficacy. In this context, the need for the introduction of flexible mechanisms, such as outcomes-based contracts and alternative payment models, is argued.

It also examines the importance of early dialogue among regulators, payers, and manufacturers, as well as the need to build specialized infrastructure and expert capacity to implement these therapies. The report emphasizes the role of international cooperation and the exchange of best practices as key factors in improving access. Emphasis is also placed on the ethical aspects related to the equitable distribution of resources and equal patient access to innovative treatments.

The recommendations addressed to the Council of Ministers, the Ministry of Health, the Bulgarian Drug Agency, the National Center for Public Health and Analyses, the National Health Insurance Fund (NHIF), and others, are extremely useful for making appropriate policy decisions to overcome barriers to access to ATMPs, which requires a systematic and coordinated approach involving regulatory reforms, innovative financing mechanisms, and the strategic development of the healthcare system.

The bibliography consists of a large number of contemporary literature sources -201.

Four scientific publications in academic journals related to the dissertation are presented; in three of them, S. Bankovski is the first author.

The content and quality of the abstract meet the requirements and reflect the main results achieved in the dissertation.

All recommendations given upon the candidate's admission and during the preliminary defense have been followed.

The work is distinguished by its thoroughness. The doctoral candidate's personal contribution is indisputable, and the formulated contributions and results achieved are his own. The work is written in a stylistically excellent and accessible language.

Conclusion: The topic is undoubtedly highly relevant, with the study focusing on access to gene and cell therapies as innovative health technologies. The study can serve as a theoretical foundation for future scientific research and for comparative analysis over time. The work has both scientific and practical relevance.

The dissertation demonstrates that Dr. Stamen Bankovski possesses the necessary knowledge, professional, and personal qualities to independently conduct scientific research, as well as to thoroughly search for and interpret data from the literature and from his own studies.

The dissertation meets all requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria and its Implementing Regulations, as well as the Regulations on the Conditions and Procedures for Acquiring Academic Degrees and Holding Academic Positions at the National Center for Public Health and Analyses (NCPHA) for the award of the educational and academic degree of "Doctor" in the scientific specialty "Social Medicine and Health Management."

The considerations set forth above give me reason to confidently give my positive assessment of the dissertation and to propose to the esteemed members of the academic jury that they award the educational and scientific degree of "Doctor" to Dr. Stamen Georgiev Bankovski in the specialty "Social Medicine and Health Management."

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May 11, 2026 ..Assoc. Prof. N. Danova, MD: